UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,856	09/09/2003	Gary R. Grotendorst	FIBRO1130-3	3430

7590 12/15/2008

Lisa A. Haile, J.D., Ph.D.
GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133

EXAMINER	
SPECTOR, LORRAINE	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
12/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/658,856	GROTENDORST ET AL.	
	Examiner	Art Unit	
	Lorraine Spector	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,19-23 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,19-23 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 15, 19-23 and 37 are pending and under consideration. Claim 15 has been amended.

Specification

The new title of the invention is not acknowledged.

Claim Interpretation

It is noted that the claims as amended are drawn to antibodies that bind to a C-terminal fragment of CTGF consisting of residues 252-349 of the full-length protein (which terminates at residue 349), that represents exon V of the full-length protein.

It is noted that since collagen synthesis is induced by the N-terminal portion of CTGF, that an antibody to exon V would inherently not inhibit collagen synthesis.

Rejections over Prior Art

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15, 19, 21-23 and 37 under 35 U.S.C. §103 as being obvious over Grotendorst et al., U.S. Patent Number 5,408,040, cited by applicants in view of U.S. Patent No.6,063,903 (Bartley et al.). Whereas Grotendorst and Neff are the inventors of the instant application, the patent names Grotendorst and Bradham, Jr. as inventors. Grotendorst et al. teaches antibodies which specifically bind to CTGF, but not to PDGF; see claims 2-4. The antibodies may also be monoclonal or polyclonal. At column 5, lines 37-45, it is disclosed that antigenic fragments may

be used to make antibodies. At column 6 Grotendorst teaches pharmaceutical uses for the antibodies for treating humans, thus anticipating claim 23 (see lines 16-22), radiolabeled antibodies (lines 34-35) and functional fragments of the antibodies (lines 47-50). At column 7, it is disclosed that goat antibodies were made to synthetic peptides containing the carboxyl sequences of the PDGF protein (as pointed out by applicants), which antibodies bound to CTGF; this is how CTGF was first isolated. The most reasonable interpretation of "peptides containing the carboxyl sequences" is that the peptides comprised some length fragement that extended to the C terminus of PDGF The carboxyl terminus of SEQ ID NO: 4 corresponds to the carboxyl terminus of PDGF. Also at column 7 and extending to column 8, is the teaching that anti-PDGF antibodies may be used to isolate PDGF on an immunoaffinity column.

Paragraph DETX(19) of the '040 patent states:

> The invention provides antibodies which are specifically reactive with CTGF polypeptide or fragments thereof. Although this polypeptide is cross reactive with antibodies to PDGF, not all antibodies to CTGF will also be reactive with PDGF. Antibody which consists essentially of pooled monoclonal antibodies with different epitopic specificities, as well as distinct monoclonal antibody preparations are provided. Monoclonal antibodies are made from antigen containing fragments of the protein by methods well known in the art (Kohler, et al., Nature, 256:495, 1975; Current Protocols in Molecular Biology, Ausubel, et al., ed., 1989). *Monoclonal antibodies specific for CTGF can be selected, for example, by screening for hybridoma culture supernatants which react with CTGF, but do not react with PDGF. (Emphasis added.)*

This, taken with the teachings of making antibodies to the terminal portions of PDGF, fairly puts into the hands of the public antibodies that bind to the C-terminus of CTGF, compositions thereof, and methods of using such, including use on an immunoaffinity column for the purpose of isolating CTGF. Thus, the '408 patent puts into the hands of the public antibodies to the C-terminus of CTGF, via it's teachings of making monoclonal and polyclonal antibodies to CTGF, and the teaching of making antibodies to synthetic peptide fragments of PDGF, a clearly analogous protein.

The '408 patent would not lead one to specifically make antibodies only to residues 75-172 of SEQ ID NO: 4.

It was well known in the art at the time the invention was made to make antibodies to a C-terminal peptide of a given protein. For example, Bartley et al. teach the production of

antibodies to the C-terminal 12 amino acids of the HEK4 receptor. (In this particular case, the antibodies were purified by passing them over a column to which the antigen had been immobilized, but that is not pertinent here.) The antibodies were able to specifically recognize HEK4 receptor by Western blots; See column 15.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to combine the teachings of Grotendorst and Bartley to make antibodies to the C-terminal 12 amino acids of CTGF. The person of ordinary skill in the art would have been motivated to do so to use the antibodies to isolate CTGF using an immunoaffinity column as was well known in the art at the time the invention was made and is taught for PDGF by Grotendorst et al., and to use the antibodies to detect CTGF in Western blots, as is taught by Bartley et al. It is further noted that as the last 12 residues of CTGF do not correspond to PDGF, nor is there any similar sequence in PDGF, that such antibodies would inherently bind to CTGF but not to PDGF.

With respect to the limitation that the antibody inhibit DNA synthesis, the Examiner cannot determine whether an antibody to the terminal 12 amino acids would inherently possess that function; it would depend on the secondary structure of exon V, and what portion(s) of exon V are responsible for that function, which is not disclosed. Since the Office does not have the facilities for examining and comparing applicants' protein with the protein of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the antibody rendered obvious by the prior art would not possess the same material functional characteristic of the claimed antibody). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

A portion of the traversal filed in the submission of 10/3/08 is pertinent here. At page 8, applicants argue that the claimed invention is based on the discovery that particular fragments of CTGF have particular biological activities. This argument has been fully considered but is not deemed persuasive. While such an argument might be persuasive if the claims were drawn to a method, they are not persuasive as regards the claimed antibodies. The art does not have to teach the same motivation or use as applicants in order for the antibodies to be obvious. The Examiner's position is supported by the case law; in *in re Swinehart and Sfiligoj*-169 USPQ

226, it was stated that "Mere recitation of a newly discovered function or property, inherently possessed by things in prior art, does not cause claim drawn to those things to distinguish over prior art. additionally, it was found that where the Patent Office has reason to believe that a functional limitation may be inherent, it may require applicant to prove otherwise.

Accordingly, the invention as claimed is *prima facie* obvious.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Grotendorst et al. in view of Bartley et al. and further in view of Hoogenboom et al., U.S. Patent No.5,565,332.

The teachings of Grotendorst et al. and Bartley are summarized above. Grotendorst and Bartley do not specifically teach human antibodies.

Hoogenboom et al. disclose human and humanized antibodies and methods of making such. At col. 1 lines 16-30 they disclose the advantages of such as being overcoming the problem of elicitation of anti-globulin response when a non-human antibody is administered to a human. See also col. 3 lines 8-15 in this regard. At col. 2 lines 57+, they disclose that antibody fragments can perform the function of whole antibodies, and set forth single chain antibodies as being examples of antibody fragments.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to substitute the anti-CTGF antibodies of Grotendorst into the human or humanized antibodies of Hoogenboom et al. to attain the known and expected advantages of such as set forth by the secondary reference and as discussed above. The person of ordinary skill in the art would expect such antibodies to function at least as well in immunopurification or Western blots as any other antibodies reactive with the same fragment. Further, having CTGF specific antibodies in hand, and given the disclosure of Grotendorst of the properties of CTGF and the suggestion that antibodies thereto be used in clinical application, there is ample motivation to make humanized antibodies as taught by Hoogenboom.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15, 19, 21-23 and 37 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-4 of U.S. Patent No. 5,408,040 in view of Bartley et al. Although the conflicting claims are not identical, they are not patentably distinct from each other for reasons cited in the above rejection under 35 U.S.C. §103(a).

Claim 20 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-4 of U.S. Patent No. 5,408,040 in view of Bartley et al. and further in view of Hoogenboom et al., U.S. Patent No. 5,565,332. for reasons cited above.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 3:00 P.M. at telephone number 571-272-0893.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's supervisor, Dr. Manjunath Rao, at telephone number 571-272-0939.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to **571-273-8300**. Faxed draft or informal communications with the examiner should be directed to ***571-273-0893.***

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lorraine Spector/ , Ph.D.
Primary Examiner
Art Unit 1647